Inhibace®

Cilazapril

Composition

Active substance: anhydrous cilazapril as cilazapril monohydrate

Excipients: excipients for coated tablets.

The film-coated tablets contain lactose.

Pharmaceutical form and quantity of active substance per unit

Inhibace submite 1 mg: Light-yellow, scored, film-coated tablets containing 1 mg anhydrous cilazapril

Inhibace mite 2.5 mg: Pink, scored, film-coated tablets containing 2.5 mg anhydrous cilazapril

Inhibace 5 mg: Reddish-brown, scored, film-coated tablets containing 5 mg anhydrous cilazapril.

Indications and potential uses

Treatment of hypertension and severe heart failure (NYHA classes III and IV).

Dosage and administration

General remarks

Inhibace should be administered once daily. As food intake has no clinically significant influence on absorption, the patient can take Inhibace before or during a meal. The product should always be taken at about the same time of day.

Hypertension

The recommended initial dosage is 1.0–1.25 mg once daily. The standard dosage of Inhibace is 2.5–5 mg once daily. Dosage should be individually adjusted according to blood pressure response. The full therapeutic effect generally appears only after 2 to 4 weeks.

Severe heart failure (NYHA classes III and IV)

Initial dosage

Therapy with Inhibace should be initiated with the recommended starting dose of 0.5 mg once daily under medical supervision.

Maintenance dosage

The dose is then increased to the lowest maintenance dose of 1 mg once daily according to tolerability and clinical status.

During maintenance therapy, further titration within the maintenance dose range of 1–2.5 mg once daily should be carried out based on tolerability and clinical status.

The usual maximum dose is 5 mg once daily.

Results from clinical trials have shown that the elimination of cilazaprilat in patients with severe heart failure correlates with creatinine clearance. Thus, special dosage recommendations should be observed in patients with severe heart failure and impaired renal function (see *Special dosage instructions* and *Pharmacokinetics*, *Pharmacokinetics in special patient groups*).

Special dosage instructions

Patients with an activated renin-angiotensin-aldosterone system (RAAS)

Particular caution is required in patients with an activated RAAS. This may be the case, for example, in renovascular hypertension or other severe forms of hypertension, hypovolemia, cardiac decompensation or concomitant vasodilator or diuretic treatment. An excessive drop in blood pressure may occur in such patients after the initial dose. For this reason a lower starting dose of 0.5 mg once daily is recommended in such patients. Salt and/or volume depletion and cardiac decompensation should be corrected before starting treatment. In hypertensive patients, diuretics should be suspended for 2–3 days before the initial dosage of Inhibace. Treatment should be initiated under medical supervision.

Patients with renal impairment

Dosage in patients with renal impairment should be reduced on the basis of creatinine clearance according to the following schedule:

Creatinine clearance	Initial Inhibace dose	Maximum Inhibace dose
>40 ml/min	1 mg once daily	5 mg once daily
10–40 ml/min	0.5 mg once daily	2.5 mg once daily
<10 ml/min	Not recommended	

In patients requiring hemodialysis, Inhibace should be administered on those days on which dialysis is not performed. Dosage should be adjusted in accordance with the blood pressure response to the drug. As with other ACE inhibitors, the likelihood of anaphylactoid reactions is increased with the use of polyacrylonitrile membranes (‘AN69’). This combination must therefore be avoided by using either other antihypertensives or other membranes for hemodialysis.

Patients with liver cirrhosis

In patients with liver cirrhosis (but without ascites) who require therapy for hypertension, Inhibace should be dosed with great caution. The dose should not exceed 0.5 mg/day and the patient’s blood pressure should be carefully monitored, as significant hypotension may occur.

Elderly patients with hypertension

Treatment should be initiated with Inhibace 0.5-1 mg once daily, depending on the patient's fluid balance and general condition. The maintenance dose should then be adjusted to the patient's individual response.

Elderly patients with chronic heart failure

In elderly patients with chronic heart failure (NYHA classes III and IV) receiving high diuretic doses, it is absolutely mandatory to only start treatment at a dosage of 0.5 mg.

Children and adolescents

see *Contraindications*.

Contraindications

Inhibace is contraindicated:

· in patients hypersensitive to the active substance cilazapril or to any of the constituent excipients or to other ACE inhibitors;

· in patients with a history of angioedema associated with previous ACE inhibitor therapy and in patients with hereditary or idiopathic angioedema;

· during pregnancy and lactation (see *Pregnancy and lactation*);

· In combination with aliskiren in patients with diabetes mellitus (type 1 and type 2) and patients with renal impairment (GFR <60 ml/min/1.73 m^2).

Efficacy and tolerability have not been studied in children or adolescents. Inhibace should therefore not be used in children or adolescents.

Warnings and precautions

Hypersensitivity and angioedema

Angioedema may occur on ACE inhibitor treatment. The reported incidence is 0.1–0.5%. Angioedema due to ACE inhibitors can present as recurrent episodes of facial swelling, which resolves on withdrawal, or as acute oropharyngeal edema and potentially life-threatening airways obstruction requiring emergency treatment. A possible variant form is angioedema of the intestine, which tends to occur within the first 24–48 hours of treatment. Patients with a history of angioedema unrelated to ACE inhibitors may be at greater risk (see *Contraindications*).

Treatment with Inhibace must be discontinued as soon as angioedema appears on the extremities, face, lips, tongue, glottis and/or larynx. The patient must be monitored closely until the swelling subsides.

Anaphylaxis

Hemodialysis

Anaphylaxis has occurred in patients dialysed with high-flux membranes (e.g. AN 69) receiving ACE inhibitors. Consideration should be given to using a different type of dialysis membrane or different class of antihypertensive agent in such patients.

Low-density lipoprotein (LDL) apheresis

Patients receiving ACE inhibitors during LDL apheresis with dextran sulphate have experienced life-threatening anaphylaxis. ACE inhibitor therapy should therefore be temporarily withheld prior to each apheresis.

Desensitization

Anaphylactic reactions can occur in patients undergoing desensitization therapy with wasp or bee venom while receiving an ACE inhibitor. Inhibace must be stopped before the start of desensitization therapy and should not be replaced by a beta-blocker.

Hematological disorders

Thrombocytopenia, neutropenia and agranulocytosis have been associated with ACE inhibitors. Agranulocytosis has been especially reported in patients with renal impairment, collagen vascular disease or those receiving immunosuppressive therapy. Periodic monitoring of the leukocyte count is therefore particularly recommended in such patients.

Aortic stenosis and hypertrophic cardiomyopathy

ACE inhibitors should be used with caution in patients with obstructive cardiac disorders (e.g. mitral stenosis, aortic stenosis, hypertrophic cardiomyopathy), since cardiac output cannot increase to compensate for systemic vasodilatation, and there is a risk of severe hypotension.

Hypotension

ACE inhibitors may cause severe hypotension, especially when starting treatment. First-dose hypotension is most likely to occur in patients with an activated RAAS. This is commonly the case in patients with renovascular hypertension, for example, or other severe forms of hypertension, hypovolemia, cardiac decompensation or concomitant diuretic or vasodilator therapy. An excessive drop in blood pressure may occur in such patients after the initial dose. For this reason a lower starting dose is recommended in such patients. Salt and/or volume depletion and cardiac decompensation should be corrected before starting treatment. Treatment should be initiated under medical supervision (see *Dosage and administration*).

Similar precautions should be taken for patients with angina pectoris or cerebrovascular disease, in whom hypotension can cause myocardial or cerebral ischemia.

Liver cirrhosis and liver damage

In patients with liver cirrhosis (but without ascites) who require therapy for hypertension, Inhibace should be initiated at a lower dose and with great caution because significant hypotension may occur. In patients with ascites, Inhibace administration is not recommended (see *Special dosage instructions*).

Liver function disorders have occurred, such as increased liver function parameters (transaminases, bilirubin, alkaline phosphatase, gamma GT) and cholestatic hepatitis. Patients receiving Inhibace who develop jaundice or marked elevations of hepatic enzymes should discontinue treatment and receive appropriate medical follow-up.

Renal impairment

Patients with renal impairment may require lower doses, depending on their creatinine clearance (see *Special dosage instructions*). Treatment with ACE inhibitors may produce increases in blood urea nitrogen and/or serum creatinine. Although these changes are usually reversible on discontinuing Inhibace and/or the diuretic, cases of severe renal dysfunction and, more rarely, acute renal failure have been reported.

Patients with renal artery stenosis, in particular, are at increased risk of developing renal impairment, including acute renal failure, during treatment with Inhibace. Caution is therefore advised when treating such patients.

Renal function should be monitored during the first weeks of therapy in these patient populations. If clinically relevant deterioration occurs in renal function, treatment should be withdrawn.

"Dual blockade" of the renin-angiotensin-aldosterone system

See *Interactions*.

Serum potassium

ACE inhibitors can cause hyperkalemia because they inhibit the release of aldosterone. This effect is usually not significant in patients with normal renal function. However, in patients with impaired renal function and/or in patients taking potassium supplements (including salt substitutes) or potassium-sparing diuretics, and especially aldosterone antagonists, hyperkalemia can occur. Serum potassium and renal function should therefore be regularly monitored. Potassium-sparing diuretics should be used only with particular caution in patients receiving a concomitant ACE inhibitor.

Surgery, anesthesia

Anesthetic agents with blood pressure-lowering effects can cause hypotension in patients receiving ACE inhibitors.

Diabetes

ACE inhibitor administration to patients with diabetes, especially those with renal impairment, may potentiate the blood glucose-lowering effect of oral hypoglycemic agents or insulin. In such patients, blood glucose levels should be carefully monitored during initiation of treatment with Inhibace.

Lactose intolerance

The formulation contains lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should therefore not take this medicinal product.

Ethnicity

ACE inhibitors have been described as less effective as antihypertensives in patients of African origin with black skin colour. An increased risk of angioedema has been described in patients with black skin colour.

Interactions

Other antihypertensive agents

An additive effect may be observed when Inhibace is administered in combination with other blood pressure-lowering agents.

Lithium

Reversible increases in serum lithium concentrations have occurred during concomitant administration of lithium with ACE inhibitors. Concomitant use of thiazide diuretics may increase the risk of lithium toxicity and enhance the already increased risk of lithium toxicity with ACE inhibitors. Coadministration of Inhibace and lithium is not recommended; however, if the combination proves necessary, serum lithium levels should be carefully monitored.

Potassium supplements, potassium-sparing diuretics, and drugs affecting serum potassium levels

The risk of developing hyperkalemia may be increased on combination therapy with ACE inhibitors and potassium-sparing diuretics (e.g. spironolactone, triamterene, or amiloride), potassium supplements, or potassium-containing solutions for infusion. Therefore, the combination of Inhibace with the above-mentioned drugs is not recommended (see *Warnings and precautions*). If potassium supplementation is indicated, it should be undertaken with caution and frequent monitoring of potassium levels.

Caution is also required when combining ACE inhibitors with drugs that may increase serum potassium levels, for example heparin.

Diuretics (thiazide or loop diuretics)

Prior treatment with high-dose diuretics may result in volume depletion and hence a risk of hypotension when initiating therapy with Inhibace (see *Warnings and precautions*). The hypotensive effect can be reduced by discontinuing the diuretic, by increasing volume or salt intake or by initiating therapy with a low dose of Inhibace.

Tricyclic antidepressants, antipsychotics, anesthetics or narcotics

Concomitant use of general anesthetics, tricyclic antidepressants and antipsychotics with ACE inhibitors may lead to further blood pressure reduction (see *Warnings and precautions*).

Non-steroidal anti-inflammatory drugs (NSAIDs) including cyclooxygenase (COX) inhibitors and aspirin ≥3 g/day

NSAID administration may attenuate the antihypertensive effect of ACE inhibitors. In elderly patients, patients with renal impairment and those with hypovolemia (including on diuretic therapy), NSAID administration with an ACE inhibitor may increase the risk of worsening of renal function (including acute renal failure) and an increased serum potassium. In such patients these drugs should therefore only be coadministered with caution and the monitoring of renal function and potassium.

Sympathomimetics

Sympathomimetics may reduce the antihypertensive effects of ACE inhibitors.

Antidiabetics

Epidemiological studies have suggested that concomitant administration of ACE inhibitors and antidiabetic medicines (insulins, oral hypoglycemic agents) may cause an increased blood glucose-lowering effect with the risk of hypoglycemia. This phenomenon appears more likely to occur during the first weeks of combined treatment and in patients with renal impairment.

Gold

Nitritoid reactions (symptoms include facial flushing, nausea, vomiting and hypotension) have been reported rarely in patients on therapy with injectable gold (sodium aurothiomalate) and concomitant ACE inhibitor therapy.

"Dual blockade" of the renin-angiotensin-aldosterone (RAA) system with ACE inhibitor (ACEI), angiotensin II receptor blocker (ARB) or aliskiren

Hypotension, syncope, hyperkalemia and renal impairment (including acute renal failure) have been observed more frequently on "dual blockade" of the RAA system with ARBs, ACEIs or aliskiren compared to monotherapy with these agents, especially in normotensive to hypotensive patients at the start of treatment.

Dual RAA system blockade should be limited to individually defined patients with monitoring of blood pressure, serum potassium and renal function.

Concomitant use of Inhibace with aliskiren is not recommended. The combination is contraindicated in certain patients with diabetes mellitus and in patients with renal impairment (see *Contraindications*).

Other medicinal products

No increase in plasma digoxin levels occurred on coadministration of Inhibace with digoxin. No clinically significant drug-drug interactions were observed when Inhibace was coadministered with nitrates, coumarin anticoagulants, and H_2 receptor blockers. There were no significant pharmacokinetic drug-drug interactions between Inhibace and furosemide or thiazides.

Hypersensitivity reactions (anaphylactoid reactions) in connection with dialysis have been described following concomitant use of ACE inhibitors and certain hemodialysis membranes (e.g. polyacrylonitrile methallyl sulphate membranes or LDL apheresis with dextran sulphate) (see *Warnings and precautions*).

Pregnancy and lactation

Pregnancy

Inhibace is contraindicated in pregnant women (see *Contraindications*).

Patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. If pregnancy is diagnosed,

Inhibace treatment should be stopped immediately and alternative therapy started if required.

Fetal exposure to ACE inhibitors during the first trimester of pregnancy has been associated with an increased risk of malformations of the cardiovascular system (atrial and/or ventricular septal defect, pulmonary stenosis, patent ductus arteriosus), central nervous system (microcephaly, spina bifida) and kidneys.

Fetal exposure to ACE inhibitor therapy during the second and third trimesters of pregnancy is known to induce human fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalemia). Should exposure to ACE inhibitors have occurred from the second trimester of pregnancy, ultrasound examination of renal function and skull is recommended. Infants whose mothers have taken ACE inhibitors should be closely observed for hypotension.

Lactation

Data from animal studies show that cilazapril is excreted in the milk of rats. No information is available in humans on the safety of cilazapril during breastfeeding. Inhibace must not be administered to the nursing mother (see *Contraindications*). Alternative treatments with better established safety profiles are preferable during breast-feeding.

Effects on ability to drive and use machines

Differences in individual response mean that Inhibace may influence the ability to drive or operate machinery. For example, dizziness, headache and fatigue may occasionally occur, especially when starting therapy (see *Warnings and precautions* and *Undesirable effects*), increasing the dose, changing medication or in conjunction with alcohol.

Undesirable effects

The most frequently reported undesirable effects in patients taking Inhibace for hypertension were headache and dizziness. In patients with chronic heart failure taking Inhibace dizziness and cough were the undesirable effects most frequently observed.

The following undesirable effects have been observed in association with cilazapril and/or other ACE inhibitors. The frequencies are based on clinical studies (very common [³ 1/10], common [>1/100, <1/10], uncommon [>1/1000, <1/100] and rare [>1/10,000, <1/1000]), and on postmarketing experience (very rare undesirable effects):

Blood and lymphatic system

Rare: Neutropenia, agranulocytosis,thrombocytopenia, anemia.

Immune system

Uncommon: Angioedema (may involve the face, lips, tongue, larynx or gastrointestinal tract) (see *Warnings and precautions*).

Rare: Anaphylaxis (see *Warnings and precautions*), lupus-like syndrome (signs and symptoms may include vasculitis, myalgia, arthralgia/arthritis, positive antinuclear antibodies, increased erythrocyte sedimentation rate, eosinophilia and leukocytosis).

Nervous system

Common: Headache.

Uncommon: Dysgeusia.

Rare: Transient ischemic attack, ischemic stroke.

Cardiovascular system

Uncommon: Angina pectoris tachycardia, palpitations, syncope.

Rare: Myocardial infarction.

Blood vessels

Common: Dizziness, lightheadedness.

Uncommon: Hypotension (see *Warnings and precautions*).

Respiratory organs

Common: Cough.

Gastrointestinal disorders

Common: Nausea.

Uncommon: Vomiting, diarrhea.

Rare: Pancreatitis

Liver and biliary tract

Rare: Elevated liver function parameters (including transaminases, bilirubin, alkaline phosphatase, gamma GT) and cholestatic hepatitis with or without necrosis.

Skin

Uncommon: Rash, pruritus.

Rare: Toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome, erythema multiforme, pemphigus, bullous pemphigoid, exfoliative dermatitis, psoriasiform dermatitis, psoriasis (exacerbation), lichen planus, urticaria, vasculitis/purpura, photosensitivity reactions, alopecia, onycholysis

Kidneys and urinary tract, electrolytes

Rare: Renal impairment, acute renal failure, blood creatinine increased, blood urea increased, hyperkalemia, hyponatremia/SIADH.

General disorders

Common: Fatigue.

Hypotension may occur when starting treatment or increasing dose, especially in at-risk patients (see *Warnings and precautions*). Hypotensive symptoms may include syncope, weakness, dizziness and visual disturbances.

Renal impairment and acute renal failure occur more commonly in patients with severe heart failure, renal artery stenosis, pre-existing renal disorders or volume depletion (see *Warnings and precautions*).

Hyperkalemia is most likely to occur in patients with renal impairment and those taking potassium-sparing diuretics or potassium supplements.

The events of transient ischemic attack and ischemic stroke reported rarely in association with ACE inhibitors may be related to hypotension in patients with underlying cerebrovascular disease. Similarly, myocardial ischemia may be related to hypotension in patients with underlying ischemic heart disease.

Overdose

Limited data are available for overdosage in humans. Symptoms associated with overdosage of ACE inhibitors may include hypotension, circulatory shock, electrolyte disturbances, renal failure, hyperventilation, tachycardia, palpitations, bradycardia, dizziness, anxiety and cough.

Suitable patient management measures are indicated in the case of overdose. Vital signs, serum electrolytes and renal function should be monitored closely and, where appropriate, continuously.

If necessary, cilazaprilat, the active form of cilazapril, may be removed from the circulation by hemodialysis (see *Warnings and precautions*).

Properties and effects

ATC code: C09AA08

Mechanism of action and pharmacodynamics

After oral administration, the active substance cilazapril is converted to cilazaprilat. Cilazaprilat intervenes in the RAAS by inhibiting the enzyme converting inactive angiotensin I to active angiotensin II, thereby decreasing the activity of angiotensin II, a potent vasoconstrictor.

At the recommended dosage the effect of Inhibace in hypertensives and patients with severe heart failure (NYHA classes III and IV) is maintained for up to 24 hours.

Clinical efficacy

Hypertension

Inhibace is effective in all grades of essential and renal hypertension, generally as monotherapy. Inhibace reduces both supine and standing systolic and diastolic blood pressure. If it is insufficiently effective, it may be combined with other antihypertensive drugs, for example non-potassium-sparing diuretics, beta blockers or calcium antagonists.

The antihypertensive effect of Inhibace is usually apparent within one hour of dosing, with maximum effect observed after 3 to 7 hours. In general, the heart rate remains unchanged. The drug does not cause reflex tachycardia, although small, clinically insignificant alterations of heart rate may occur.

At recommended doses the antihypertensive effect of Inhibace is maintained for up to 24 hours. In some patients, blood pressure reduction may diminish towards the end of the dosage interval. The antihypertensive effect of Inhibace is maintained during long-term therapy. No rapid increase in blood pressure has been observed after abrupt withdrawal of Inhibace.

Severe heart failure (NYHA classes III and IV)

In patients with severe heart failure the RAAS and sympathetic nervous system are generally activated, leading to enhanced systemic vasoconstriction and increased sodium and water retention. By suppressing the RAAS, Inhibace improves the filling conditions of the failing heart by reducing systemic vascular resistance (afterload) and pulmonary capillary wedge pressure (preload) in patients receiving diuretics and/or digitalis. It increases exercise tolerance in these patients, who experience this as improved quality of life. The hemodynamic and clinical effects appear promptly and persist.

Pharmacokinetics

Absorption

Cilazapril is well absorbed and rapidly converted to the active form, cilazaprilat. If the patient eats immediately before Inhibace administration, absorption is slightly delayed and reduced (by 15%), but this is of no therapeutic importance. The bioavailability of cilazaprilat, as measured on the basis of urinary excretion, is approximately 60%. Maximum plasma concentrations are reached within 2 hours of administration and are proportional to dose.

Metabolism

Cilazaprilat is excreted unchanged by the kidneys.

Elimination

The drug undergoes biphasic elimination, with half-lives of 2 and 40 hours. The effective half-life (i.e. the half-life that determines time to steady state) is 9 hours during once-daily dosing with Inhibace.

Patients with renal impairment: see *Pharmacokinetics in special patient groups*.

Pharmacokinetics in special patient groups

In patients with renal impairment, higher plasma concentrations of cilazaprilat are observed than in patients with normal renal function, since drug elimination decreases in proportion to declining creatinine clearance. There is no elimination in patients with end-stage renal failure, but hemodialysis reduces concentrations of both cilazapril and cilazaprilat to a limited extent (see *Special dosage instructions*).

In elderly patients whose renal function is normal for age, plasma cilazaprilat levels may be up to 40% higher than in younger patients, with elimination reduced in keeping with the lower creatinine clearance. Similar pharmacokinetic changes occur in patients with moderate to severe liver cirrhosis (see *Special dosage instructions*).

Patients with hepatic impairment: Increased plasma levels and reduced plasma and renal clearance have been observed in patients with liver cirrhosis, with greater effects on cilazapril than on its active metabolite, cilazaprilat.

In patients with chronic heart failure, cilazaprilat elimination is dependent on renal function and correlates with creatinine clearance. Dosage adjustments are therefore indicated as for patients with impaired renal function (see *Special dosage instructions*).

Preclinical data

As with other ACE inhibitors the kidneys were the primary systemic toxicity target organ in subchronic and chronic toxicity studies. Plasma urea and creatinine levels were increased, and there was glomerular arteriolar thickening, occasionally in conjunction with juxtaglomerular cell hyperplasia. These changes were partly reversible and were due to excessive pharmacodynamic activity by cilazapril.

Carcinogenicity
The study of cilazapril in mice and rats revealed no evidence of carcinogenicity.

Mutagenicity
Cilazapril showed no mutagenic or cytotoxic effects in a variety of in-vitro and in-vivo mutagenicity tests.

Impairment of fertility
Cilazapril had no effect on fertility in male and female rats.

Teratogenicity
Cilazapril was non-teratogenic in rats and cynomolgus monkeys.

Reproductive toxicity
As with other ACE inhibitors evidence of fetotoxicity has been observed with cilazapril in reproductive toxicity studies in rats. The main findings were an increase in preimplantation loss, fewer viable fetuses, and decreased body weight. A slightly increased incidence of renal pelvis dilatation was observed in rats at doses exceeding 7 mg/kg/day.

Placental transfer
After administration of ^{14}C-labelled cilazapril to pregnant mice, rats and monkeys, radioactivity was also detectable in the fetuses.

Transfer into milk
Data from animal studies show that cilazapril is excreted in the milk of rats.

Additional information

Stability
This medicinal product must not be used after the expiry date (EXP) shown on the container.

Special instructions for storage
Do not store above 25 °C and keep out of the reach of children.

Instructions for disposal
The improper release of medicinal products into the environment should be avoided wherever possible. Do not dispose of medicinal products via the wastewater system and avoid disposal in domestic waste.

Packs

Inhibace submite
Film-coated tablets 1 mg 30

Inhibace mite
Film-coated tablets 2.5 mg 28

Inhibace
Film-coated tablets 5 mg 28

This is a medicament

A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.

Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.

The doctor and the pharmacist are experts in medicine, its benefits and risks.

Do not by yourself interrupt the period of treatment prescribed for you.

Do not repeat the same prescription without consulting your doctor.

Medicine: keep out of reach of children

Council of Arab Health Ministers

Union of Arab Pharmacists

Current at February 2014

Made for F. Hoffmann-La Roche Ltd, Basel, Switzerland
by Roche Farma SA, Leganés, Spain